REMARKS/ARGUMENTS

Applicants express their appreciation to Examiner LaCourciere for the courtesy of the interview on July 12, 2004 with Applicants' representatives, Donna Ward and Paul LeGaard.

After amendment, the pending claims are 1, 4-7, 9-10, and 12-15. Claims 8, 11, and 21-13 are canceled, without prejudice, in an effort to place the application in condition for allowance. Applicants reserve the right to prosecute these claims, and any other currently or previously canceled claims and/or subject matter, in a continuation application filed during the pendency of the present application.

Claim 1 is amended to clarify the invention. Support for this amendment is found in the originally filed specification and claims as filed. No new matter is added by this amendment.

35 USC § 112, First Paragraph Rejection

Claims 1, 4-7, 9, 10, 12-15, 21, and 22 are rejected under 35 USC § 112, first paragraph.

The Examiner asserted that support for oligonucleotides 17 and 19 nucleobases in length could not be found in the originally filed specification.

Applicants respectfully request reconsideration and withdrawal of this ground for rejection in view of the above amendments to the claims and the following remarks.

The pending claims have been amended to refer to oligonucleotide sequences 20 nucleobases in length, which embodiment is fully supported in the originally filed specification. Applicants' definition of antisense of 20

nucleobases in length is supported by the large number of examples of 20-mer antisense sequences in Table 1 at pages 85-87 of the originally filed specification. Additionally the 20-mer length falls within the range specified at page 13, lines 31-36.

In view of this amendment, this rejection may be properly withdrawn.

35 USC § 102(b) Rejections

(i) *Claims 1, 4-7, 9, 10, and 12-15 are rejected under 35 USC § 102(b) over Damha et al. (International Patent Publication No. WO 99/67378).*

The Examiner asserted that Damha discloses an 18-mer antisense compound meeting the length limitation of the amended claims.

Applicants respectfully request reconsideration and withdrawal of this ground for rejection in view of the above amendments to the claims and the following remarks.

As amended, claim 1 requires that the antisense sequence be 20 nucleobases in length. Damha provides no oligonucleotide sequences of 20 nucleobases in length that specifically hybridize with human stearoyl-CoA desaturase. Damha therefore cannot be used as a novelty reference against the presently amended claim 1, nor any of the claims dependent therefrom.

This rejection may be properly withdrawn.

(ii) *Claims 1, 4-6, 10, 12-15, and 21-23 are rejected under 35 USC § 102(b) over Beigelman (International Patent Publication No. WO 96/18736).*

The Examiner asserted that given the complementarity of the ribozyme of Biegelman to Applicants' sequence, it would be expected that the ribozyme would "fully hybridize" to the target.

Applicants respectfully request reconsideration and withdrawal of this ground for rejection in view of the above amendments to the claims and the following remarks.

As amended, claim 1 and its dependent claims require that the antisense oligonucleotide sequences be 20 nucleobases in length.

In contrast, Biegelman's ribozyme sequences contain 14 nucleotides. The sequence of Biegelman therefore does not meet the 20 nucleobase feature of the amended claims.

Based on this amendment, Biegelman cannot be used as a novelty reference against the presently amended claim 1, nor any of the claims dependent therefrom.

This rejection may be properly withdrawn.

35 USC § 103(a) Rejection

Claims 1, 4-10, 12-15, and 21-23 are rejected under 35 USC § 103(a) over Stenn et al. (International Patent Publication No. WO 00/09754) in view of Milner et al. (1997, Nat. Biotech., 15:537) and Baracchini et al. (US Patent No. 5,801,154).

The Examiner asserted that the skilled artisan would reasonably have expected to find at least one antisense oligonucleotide that inhibited the expression of stearoyl-CoA desaturase by at least 10% under some assay condition by screening for antisense against the known sequence, as claimed.

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the above amendments to the claims and the following remarks.

Applicants submit that one of skill in the art would not have reasonably expected that combining the cited references would provide the present application. Specifically, the combined references do not provide any basis for a reasonable expectation that screening will provide synthetic 20-mer antisense oligonucleotides that specifically hybridize to human stearoyl-CoA desaturase and inhibit stearoyl-CoA desaturase by greater than 10%. The combination of the above-cited three references fails to make a *prima facie* case of obviousness against the pending claims of this application.

Stenn discusses human stearoyl CoA desaturase, but does not discuss antisense sequences to human stearoyl CoA desaturase. Stenn cannot therefore suggest *20-mer* antisense oligonucleotides. Stenn provides no basis from which one of skill in the art could expect to inhibit synthesis of the desaturase enzyme by any percentage.

Baracchini discusses antisense compounds which inhibited expression of a completely different target, i.e., the ***multidrug resistance-associated protein*** (MRP). Baracchini does not discuss the human stearoyl-CoA desaturase target or that the antisense compounds discussed therein could be utilized to target expression of human stearoyl-CoA desaturase. Baracchini only provides levels of inhibition for two of the 16 exemplified antisense compounds, and provides no suggestion that similar

inhibition levels would be anticipated for any antisense sequences to any target.

Milner refers to 15- to 17-mer antisense oligonucleotides that inhibit expression of another completely different target, i.e., ***rabbit β-globin protein*** with either no specific inhibition, "complete" inhibition, or 36% inhibition. Milner does not discuss antisense sequences targeted to a nucleic acid molecule encoding human stearoyl-CoA desaturase. Milner does not suggest *20-mer* antisense sequences to any target.

With respect, the Examiner's combination of these references is not proper. To meet the requirements of Applicants' amended claims, the Examiner must take only a portion of the teachings of each reference (and nothing at all suggested by Milner) and combine them with no suggestion to do so found anywhere in the three respective documents. An obviousness rejection cannot be made by combining documents to make the bald suggestion that it is "obvious to try" to make antisense compounds to target stearoyl-CoA desaturase, simply because others have made antisense compounds to other ***unrelated*** proteins and that antisense sequences to stearoyl-CoA desaturase would be desirable, if made. The US patent law has long held that the "obvious to try" standard is not the appropriate standard for a determination of patentability.

Additionally, the mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious, unless the prior art *suggested* the desirability of the modification. As

discussed above, the prior art references in combination and taken as a whole do not suggest the claimed invention.

Nor does the combination of these references provide any *expectation of success* that if one did target the specifically claimed stearoyl-CoA desaturase SEQ ID NO: 3 sequence of the present claims, that one would obtain 20-mer antisense sequences with the desired 10% inhibitory result. These three references provide neither motivation to make and use antisense compounds capable of inhibiting stearoyl-CoA desaturase expression nor any reasonable expectation of success that such sequences capable of inhibiting the target may be achieved.

This combination of prior art, when the teachings are taken *as a whole*, does not provide any *suggestion* of the antisense sequences encompassed by Applicants' amended claims and fails to supply both the motivation and a reasonable expectation of success required to set forth obviousness of the pending claims.

The only source of the required motivation to make and use antisense compounds capable of inhibiting stearoyl-CoA desaturase expression by at least 10% is provided by the Applicants' own specification. The only teachings that supply the necessary motivation and expectation of success that such a composition would be useful are provided by the instant specification. Only Applicants have shown 20-mer antisense sequences to stearoyl CoA desaturase, that the same inhibit this target at 10% or greater, and assays for testing such targets in its specification.

In view of the above amendments and these remarks, Applicants' respectfully request that the Examiner withdraw the outstanding rejections and permit the above pending claims to pass to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,
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